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Published:

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9 September 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR REDUCING SOMATIC CELL COUNT IN MILKY ADMINISTRATION OF MUTATED ENTEROTOXINS

(57) Abstract: In an embodiment, the present invention is directed to a method of reducing the somatic cell count in milk including administering an effective amount of a toxin to a mammal. In some embodiments, the toxin administered has a modified disulfide loop region. For example, at least 40% of the amino acid residues within the disulfide loop region are deleted in some embodiments. The mammal reacts to the administered toxin with an immune response. In an embodiment, the present invention is directed a method of increasing the quality of milk produced by mammals including administering an effective amount of a toxin to a mammal.

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INTERNATIONAL SEARCH REPORT

Inte

Application No

PCT/US2005/000482

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K39/085 A61K39/09 A61P31/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, FSTA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|------------------------|
| X | WO 01/60851 A (LG CHEMICAL LTD; LEE, HONG-KYUN; PARK, YONG-HO; HAN, KYU-BOEM; CHANG,) 23 August 2001 (2001-08-23) | 1, 2, 4, 5, 7-9, 11-17 |
| Y | page 3, lines 10-17 page 4, lines 5-15 page 5, line 23 - page 6, line 6 page 23, line 14 - page 27 | 10 |
| Y | WO 99/27889 A (IDAHO RESEARCH FOUNDATION, INC; BOHACH, GREGORY, I) 10 June 1999 (1999-06-10) cited in the application abstract page 5, lines 12-26 page 6, lines 23-33 page 8, lines 1-24 example 2; table 4 | 10 |

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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

21 July 2005

Date of mailing of the international search report

29/07/2005

Name and mailing address of the ISA

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Noë, V

INTERNATIONAL SEARCH REPORT

Intern: Application No
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| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|---|-----------------------|
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| A | <p>HOVDE C J ET AL: "INVESTIGATION OF THE ROLE OF THE DISULPHIDE BOND IN THE ACTIVITY AND STRUCTURE OF STAPHYLOCOCCAL ENTEROTOXIN C1" MOLECULAR MICROBIOLOGY, BLACKWELL SCIENTIFIC, OXFORD, GB, vol. 13, no. 5, 1994, pages 897-909, XP002067000 ISSN: 0950-382X the whole document</p> | |

INTERNATIONAL SEARCH REPORT

Int'l application No.

PCT/US2005/000482

Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
- a. type of material
- ☒ a sequence listing
- ☐ table(s) related to the sequence listing
- b. format of material
- ☒ in written format
- ☒ in computer readable form
- c. time of filing/furnishing
- ☐ contained in the international application as filed
- ☐ filed together with the international application in computer readable form
- ☒ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-17 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 1-17 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Present claims 1-4,9,11-13,15-17 relate to an large number of possible methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be disclosed, namely those parts relating to the methods comprising administering disulfide loop region deletion mutants from staphylococcal enterotoxins or from Streptococcus pyrogenes toxins (see page 4, line 25 - page 5, line 6).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

tion on patent family members

Internat I Application No
PCT/US2005/000482

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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